

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application.

#### **Listing of Claims:**

1. – 3. (Canceled)

4. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH

additionally containing an N-terminal methionine; and

wherein the hGH:polyarginine ratio is 12:1 to 3:1 (w/w).

5. – 6. (Canceled)

7. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH

additionally containing an N-terminal methionine;

wherein the hGH:polyarginine ratio is 12:1 to 3:1 (w/w); and

wherein the crystal is characterized by a release profile such that a single administration of said crystal to a mammal provides an *in vivo* human growth hormone (hGH) serum

concentration profile in said mammal having a  $T^{90\%}$  value higher than that provided by a single administration of the same amount of soluble human growth hormone.

8. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH

additionally containing an N-terminal methionine;

wherein the hGH:polyarginine ratio is 12:1 to 3:1 (w/w); and

wherein the crystal is characterized by an insulin growth factor-1 (IGF-1) serum elevation profile such that a single administration of said crystal to a mammal provides an *in vivo* IGF-1 serum elevation over baseline IGF-1 level in said mammal at similar levels compared to those provided by the same amount of soluble human growth hormone (hGH) administered in more than one administration.

9. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH

additionally containing an N-terminal methionine;

wherein the hGH:polyarginine ratio is 12:1 to 3:1 (w/w); and

wherein the crystal is characterized by a bioavailability such that a single administration of said crystal has a relative bioavailability of at least 50% or more, as compared to that of an identical dose of soluble human growth hormone (hGH) delivered via the same administrative route, wherein said bioavailability is measured by area under curve (AUC) of total *in vivo* hGH serum concentration for said soluble hGH and said hGH crystal.

10. (Original) The crystal according to claim 7 or 8, wherein said mammal is a human.

11. – 16. (Canceled)

17. (Previously presented) A composition comprising the crystal according to claim 4, 7, 8 or 9, and an excipient.

18. (Previously presented) The composition according to claim 17, wherein said crystal and said excipient are present in said composition at a molar ratio of human growth hormone (hGH):excipient of 1:10 to 1:0.125.

19. (Original) The composition according to claim 17, wherein said excipient is selected from the group consisting of: amino acids, salts, alcohols, carbohydrates, proteins, lipids, surfactants, polymers, polyamino acids and mixtures thereof.

20. (Previously presented) The composition according to claim 17, wherein said excipient is selected from the group consisting of: protamine, polyvinylalcohol, cyclodextrins, dextrans, calcium gluconate, polyamino acids, polyethylene glycol, dendrimers, polyorthinine, polyethyleneimine, chitosan and mixtures thereof.

21. (Original) The composition according to claim 20, wherein said excipient is selected from the group consisting of: protamine, polyarginine, polyethylene glycol and mixtures thereof.

22. (Previously presented) The composition according to claim 17, wherein the concentration of human growth hormone (hGH) in said composition is between 0.1 and 100 mg/ml.

23. – 59. (Canceled)

60. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the polyarginine is co-crystallized with the human growth hormone (hGH).

61. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the polyarginine is complexed with crystals of the human growth hormone (hGH).

62. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the crystal is produced by co-crystallizing the human growth hormone with polyarginine.

63. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the crystal is produced by:

- (a) crystallizing the human growth hormone, and
- (b) complexing polyarginine to the crystallized human growth hormone.

64. (Previously presented) The polyarginine containing crystal according to claim 4, further comprising a cation.

65. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 4.

66. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 7.

67. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 8.

68. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 9.

69. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 60.

70. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 61.

71. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 62.

72. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 63.

73. (Previously presented) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 64.

74. (Previously presented) The polyarginine containing crystal according to claim 7, further comprising a cation.

75. (Previously presented) The polyarginine containing crystal according to claim 8, further comprising a cation.

76. (Previously presented) The polyarginine containing crystal according to claim 9, further comprising a cation.

77. (Previously presented) The polyarginine containing crystal according to claim 60, further comprising a cation.

78. (Previously presented) The polyarginine containing crystal according to claim 61, further comprising a cation.

79. (Previously presented) The polyarginine containing crystal according to claim 62, further comprising a cation.

80. (Previously presented) The polyarginine containing crystal according to claim 63, further comprising a cation.

81. (New) The polyarginine containing crystal according to claim 4, wherein the hGH:polyarginine ratio is 5:1 (w/w).

82. (New) The polyarginine containing crystal according to claim 7, wherein the hGH:polyarginine ratio is 5:1 (w/w).

83. (New) The polyarginine containing crystal according to claim 8, wherein the hGH:polyarginine ratio is 5:1 (w/w).

84. (New) The polyarginine containing crystal according to claim 9, wherein the hGH:polyarginine ratio is 5:1 (w/w).